B. Remarks

Newly added claims 54-59 do not add new matter to the application and their entry is therefore respectfully requested. Support for the newly added claims is found throughout the specification.

REMARKS

A. Status of the Claims

Claims 38 and 41-53 were pending in the case at the time of the Official Action, dated January 13, 2004. All claims stand rejected. Claims 38 and 43-53 stand rejected under 35 U.S.C. § 112, first paragraph. Claims 38 and 43-46 stand rejected under 35 U.S.C. § 102(b) as being unpatentable over Hillman *et al.* (WO 00/06728). Claims 47-53 stand rejected under 35 U.S.C. § 102(e) as being unpatentable over Fodor *et al.* (U.S. Patent No. 6,582,908). Finally, claims 38 and 43-46 stand rejected for obviousness-type double patenting over claims 1-9 of U.S. Patent No. 6,642,370.

B. Rejections Based on 35 U.S.C. § 112, First Paragraph, are Overcome

Claims 38 and 43-53 stand rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

Claims 38 and 43-46 were rejected under 35 U.S.C. § 112, first paragraph, because "claim 38 permits conservative, but undisclosed, amino acid substitutions, which would necessarily result in undisclosed nucleic acid substitutions." To begin, Applicant has revised claim 38 to more clearly set forth the scope of this claim. Applicant respectfully submits that the specification in paragraph 32, beginning on page 12, clearly describes conservative amino acid variants of both SEQ ID NO:20 and SEQ ID NO:22, and are a genus of nucleic acid molecules that are well understood by one of ordinary skill in the art. This understanding is supported by § 2144.08 of the M.P.E.P., which states that "an exemplified species may differ from a claimed species by a conservative substitution ('the

replacement in a protein of one amino acid…[which] is generally expected to lead to either no change or only a small change in the properties of the protein')," and indicates the acceptance of the premise that conservative amino acid variants maintain similar properties, and negating the Examiner's assertion that Applicant only has possession of the two mutant sequences. Applicant furthermore submits that § 2422.03 of the M.P.E.P. expressly provides that "[i]t is generally acceptable to present a single, general sequence in accordance with the sequence rules and to discuss and/or *claim* variants of that general sequence without presenting each variant as a separate sequence." Finally, it is well established that persons of ordinary skill in the art are enabled to determine and/or create nucleotide sequences that will encode a specified polypeptide. Therefore, Applicant respectfully requests withdrawal of this rejection.

Claims 47-52 were also rejected under 35 U.S.C. § 112, first paragraph, because "these claims encompass the full length gene with conservative substitutions" because of the "use of the term 'comprising'[, which] negates this as an upper bound to the nucleic acid molecule." First, the scope of these claims has been further clarified to include nucleic acid sequences that comprise *at least* about 20 contiguous nucleotides of SEQ ID NO:18. Applicant respectfully asserts that this scope was already apparent from the claims, which included nucleic acid molecules that contain both mutations set forth, because the mutations are located approximately 70 nucleotides apart.

Turning to the above rejection, conservative substitutions of amino acids is not an issue for these claims, since they are directed to specific nucleic acid molecules that are linked to a specific nucleic acid sequence, not an amino acid sequence. With respect to the "comprising" language of the claims, this language indicates that extraneous sequences, for example affinity tags, expression sequences such as promoters, viral sequences, or plasmid sequences, could be added to one or both ends of the at least about 20 contiguous nucleotides of SEQ ID NO:18 (with one or both of the

indicated mutations). One of skill in the art would clearly understand that such sequences were in the inventor's possession at the time of filing, since the construction and use of such sequences is routine in the art. Therefore, one of ordinary skill in the art would clearly understand the scope of these claims, and that Applicant was in full possession of this scope at the time the application was filed. Applicant respectfully requests withdrawal of this rejection.

Claim 53 was also rejected under 35 U.S.C. § 112, first paragraph, because "no description of the hybridizing oligonucleotides is provided and this genus is also immense." Claim 53 has been revised to clarify that the oligonucleotides encompassed by this claim are those that hybridize to the nucleic acid molecule of claim 47 but will not substantially hybridize to the corresponding region of the nucleic acid molecule consisting of SEQ ID NO:18. Therefore, this population of oligonucleotides must be able to differentially hybridize to two sequences that differ by one or two nucleotides (*i.e.*, the identified mutations). In fact, this genus will be far from immense. Therefore, Applicant respectfully requests withdrawal of this rejection.

B. Rejection Based on 35 U.S.C. § 102(b) is Overcome

Claims 38 and 43-46 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hillman because "Hillman teaches a nucleic acid molecule… which is 99% identical to SEQ ID NO:18 and encodes an amino acid sequence that comprises a conservative substitution of SEQ ID Nos: 20 and 22…"

Applicant respectfully points out that Hillman discloses the wild-type nucleic acid sequence of CD2 binding protein (see SEQ ID NO:14), which does not encode an amino acid sequence that comprises conservative substitutions of SEQ ID NO:20 or SEQ ID NO:22. As explained in paragraph 103 on page 41 of the specification, the missense mutation at nucleotide position 748 of

the CD2BP1 sequence is predicted to change negatively charged glutamic acid (E) to a polar uncharged glutamine, and the missense mutation at nucleotide position 688 of the CD2BP1 sequence is predicted to change nonpolar alanine (A) to the polar uncharged amino acid threonine (T). Neither of these changes are conservative amino acid substitution as understood by a person of ordinary skill in the art, and as set forth in the specification (see paragraph 32, beginning on page 12). Therefore, Hillman does not anticipate claims 38 or 43-46, and Applicant respectfully requests withdrawal of this rejection.

C. Rejection Based on 35 U.S.C. § 102(e) is Overcome

Claims 47-53 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Fodor because the "phrase 'about' permits some flexibility in the length of the oligonucleotide" and is deemed by the Examiner to "be a broad term which permits the 10-mer nucleic acids of Fodor to apply."

Claim 47 has been changed to indicate that the claimed nucleic acid molecule is "at least about 20" nucleotides in length, indicated that "about 20" is the lower limit of the nucleic acid molecule. As indicated by the Examiner, use of the term "about" is to permit "some flexibility" on the length of the claimed nucleic acid sequence, however, no person of ordinary skill in the art would interpret the term "about 20" to include a 10-mer, which is approximately 50% of the lower limit of the claimed value. *Some flexibility* is just that- it is not intended to give a patentee an unreasonably broad scope in light of the claimed value. Since a person of ordinary skill in the art would not interpret "about 20" to include 10-mers, Applicant asserts that Fodor does not anticipate claims 47-52, and respectfully requests withdrawal of this rejection.

Claim 53 has also been clarified to indicate that the claimed oligonucleotides must be able to differentially hybridize to two sequences that differ by one or two nucleotides (*i.e.*, the identified

mutations). Since Fodor only describes 10-mers, and the two identical mutations are over 10 nucleotides apart in the CD2BP1 sequence, a 10-mer oligonucleotide would have to be able to differentially hybridize to the nucleic acid molecule of claim 47 but not to the corresponding region of the nucleic acid molecule consisting of SEQ ID NO:18, which would only differ by a single nucleotide. A person of ordinary skill in the art understands that a 10-mer oligonucleotide simply is not long enough to reliably accomplish this task because its Tm will be too low, and therefore a 10-mer cannot be encompassed within the scope of claim 53. Therefore, Applicant respectfully requests withdrawal of this rejection.

D. Rejection Based on Double Patenting is Overcome

Claims 38 and 43-46 stand rejected for obviousness-type double patenting. The Action cites claims 1-9 of U.S. Patent No. 6,642,370 as the bases for the double patenting rejection. Applicant has attached hereto a terminal disclaimer that overcomes this basis of rejection. Texas Scottish Rite Hospital for Children owns U.S. Patent No. 6,642,370. Accordingly, Applicant respectfully requests withdrawal of this rejection for obviousness-type double patenting.

CONCLUSION

It is Applicant's belief that the claims are in condition for allowance. Such favorable action is respectfully requested. If the Examiner has any questions or comments regarding any issue associated with this application a telephone call to the undersigned representative at 512-542-8569 is welcome.

Respectfully submitted,

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Date: April 13, 2004
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